REMARKS

In view of the foregoing Amendments and following remarks, reconsideration and allowance of the present application are respectfully requested.

In general, the present invention is directed to certain fluorinated compounds. For instance, independent claim 20 is directed to certain N-alpha trifluoroethyl amino acid compounds. Another embodiment, specifically, claim 25, is directed to certain N-alpha trifluoroethyl amino acid esters, and the embodiment disclosed in claim 31 is directed to a peptide comprising a terminal N-alpha trifluoroethyl amino acid. The disclosed compounds can show efficacy in many different applications including, for example, as reaction agents in polymerization of useful amino acid structures, as biological building blocks to generate pharmaceutically useful and active compounds, as tagging or labeling compounds in forensic applications, and in anti-cancer applications, among others.

Currently, claims 20-32, and 34-47 are pending in the application, including independent claims 20, 25, and 31.

In the Office Action, claims 30, 33, and 45 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 33 has been canceled herein.

Claim 30 is directed to a composition comprising an N-alpha trifluoroethyl amino acid ester in which the terminal R2 group comprises a protein. Claim 45 is directed to a compound including an ester group in which the terminal R3 group is a protein. In the specification, at the first paragraph of page 5, the compounds of the disclosed invention are discussed in regard to the lipophilic characteristics of the compounds due to the presence of the carbofluorine group on the compounds. In particular, this paragraph discusses that proteins (such as those involved in osteoporosis, arthritis, and cancer) may be reacted with the disclosed compounds containing carbofluorine groups to produce more lipophilic structures as compared to their fully hydrogen-saturated counterparts. In addition, in the first paragraph of page 6, the specification discloses that structures embodied by the disclosed invention may be incorporated into animal or

human proteins having biological application (page 6, lines 9-11). In the specification at page 14, lines 14-18, and at page 18, lines 15-19, can be found teachings concerning the reactivity of the disclosed compounds, and in particular, the finding that the reactivity of the disclosed amino acids is reversed relative to the known N-alkyl amino acids. That is, reaction occurs only at the carboxyl group of the amino acid, under the routine conditions used for N-protected amino acids in peptide synthesis (page 18, lines 15-19). As such, Applicants respectfully submit that descriptive support for claims 30 and 45 exists in the specification as filed. Specifically, the disclosure teaches that amino acids or peptides of the invention can be combined with proteins to form novel esters, and in forming the novel esters, the combination of the two components will occur at the carboxyl end of the amino acid or the peptide.

In the Office Action, claims 20-47 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. Several specific points were addressed in the Office Action. Each specific point is addressed in turn below:

- Claims 20, 25, 32, 35, 37-39, 41-44, 46, and 47 have been amended to specifically show the hydrogen atoms on the nitrogen-containing groups.

- Both the term 'aryl' and the term 'aromatic compound' were used in the Markush grouping of claims 20, 25, 32, and 35. An aryl is by definition an organic radical derived from an aromatic hydrocarbon by removal of one hydrogen. (Dictionary of Scientific and Technical Terms, Daniel N. Lapedes, ed., McGraw-Hill Book Co., 1974.) In order to avoid the appearance of redundancy, and, as an aryl is still an aromatic, the term 'aryl' has been deleted from these claims. In addition, the term 'aromatic compound' has been amended to 'aromatic group' as requested in the Office Action.

- Previously presented claims 20, 25, 32, and 35 included the term 'heterocyclic compounds.' This term has been amended to 'heterocyclic groups' as requested in the Office Action.

- Previously presented claims 20, 25, 32, and 35 included the term 'sulfur containing alkyls.' This term has been amended to 'thioalkyl groups,' that is, a straight chain alkyl group containing one or more sulfur atoms, as requested in the Office

Action.

- Claims 20-30 are drawn to a composition. As correctly pointed out in the Office Action, a composition by definition includes two or more components. A composition is defined to be "the elements or compounds making up a material or produced from it by analysis" (Dictionary of Scientific and Technical Terms, Daniel N. Lapedes, ed., McGraw-Hill Book Co., 1974.) Thus, the components of a composition, may be the elemental components, as in the sodium and the chloride which together form the composition sodium chloride, or the compounds which go into a mixture, as in the salt and the water which together form a saline solution.

The compositions of the present invention can, in certain embodiments, include the disclosed compounds as well as other compounds, such as in a mixture. The other compounds employed can usually depend upon the application in which the disclosed compounds are to be used. For example, in one embodiment, the disclosed compounds can be useful as reaction agents in a polymerization process. When utilizing, for instance, an emulsion polymerization process, the other compounds could include the monomers to be polymerized, possibly a colloid stabilizer, and the dispersion medium, which can be either nonaqueous or aqueous, depending on the system. Thus, in this application, the other compounds in the composition will depend upon the specifics of the polymerization process.

In other applications, the disclosed compounds can be pharmaceutically useful. In this particular embodiment, the compounds could be in a form so as to be pharmaceutically active, e.g., digestible or injectable. For instance, an injectable composition would most likely be an aqueous composition and include some water.

Additional possible applications of the disclosed compounds are disclosed throughout the application, some of which may utilize the disclosed compounds in conjunction with other materials.

In other embodiments, the composition of the present invention can be the composition of matter that is the compound itself, wherein the components of the composition are the elemental components of the compound.

Therefore, because whoever discovers any new and useful composition of matter may obtain a patent therefore, subject to the conditions and requirements of title 35 (35

U.S.C. §101), and in addition, since, when read in light of the specification, claims 20-30, drawn to a composition, do particularly point out and distinctly claim the subject matter which applicant regards as the invention, Applicant respectfully submits that the presently pending claims fully comply with 35 U.S.C. §112, second paragraph.

- Claim 33, which made reference to "multiple independent n groups" has been canceled.

In the Office Action, claim 31 was rejected under 35 U.S.C. §102(b) as being anticipated by Carr, S. (*Biomedical Mass Spectrometry* **8**(2), 51-61, 1981), with specific reference to scheme 1, scheme 2, and figure 8.

Carr discloses optimization of a derivatization chemistry for the sequencing of polypeptides by gas chromatographic mass spectrometry. The derivatives of choice for the sequencing process are the N-α, (ω)-trifluoroethyl–O-trimethylsilyl poly-amino alcohols of the peptides (page 51, col. 2). The derivative illustrated in Scheme 1, however, is not a peptide. While the side chains of the original peptide may still exist, the peptide itself has been reduced, and rather than a trifluoroethyl group added to the N-terminal nitrogen of a peptide, as is found in the present invention, amino alcohols have been formed from the peptide C-termini. As can more clearly be seen in scheme 2, page 56, and as described more fully in the Experimental section beginning on page 52, the derivitazation process of Carr includes the acylation of peptides with trifluoroacetic anydride (TFAA) and trifluoroacetic acid (TFA) to form a methylated, trifluoroacylated polyamide. The polyamide thus produced is then reduced, such as with lithium aluminum deuteride or hexadeuterodiborane, to form the polyamino alcohols of the process. In the present invention, in contrast, the peptide chain can be maintained, while the N-terminal nitrogen can be protected with a trifluoroethyl group. As such, Applicants respectfully submit that claim 31 patentably defines over Carr.

In the Office Action, claim 31 was also rejected under 35 U.S.C. §103 as being unpatentable over DesMarteau, D. (*Chemical Communications (Cambridge)* (20), 2241-2242, 1998) in view of McDowell (*Biochem* 35, 3328, 1996) or Hoeltzi (*Biochem* 33, 5502, 1994) or Duewel (*Biochem* 36, 3404, 1997). DesMarteau discloses an N-epsilon trifluoroethyl amino acid and suggests that the compound may be useful for ^{19}F NMR studies. As correctly pointed out in the Office Action, DesMarteau does not disclose

amino acids bearing a trifluoroethyl group bonded to the N-alpha position as is taught in the present application. Similarly, none of the other references disclose an amino acid bearing a trifluoroethyl group bonded to the N-alpha position. All of the secondary references, similar to the primary reference, discuss the labeling of side chains of peptides for various purposes, e.g. examination of regions of a protein (Hoeltzli), to monitor positions of specific residues on ligand binding (McDowell), or to investigate the importance of methionine in biological system, (Duewel). Thus, the references are all looking to discover information concerning specific proteins or sections of proteins. As such, the references utilize a process for labeling those portions of the peptide chains which differentiate one amino acid from another (i.e., the side chains) so as to, for example, differentiate one peptide chain from others or recognize that one peptide chain in ^{19}F NMR studies.

In the Office Action, it was suggested that a skilled NMR spectroscopist would have been motivated to prepare a peptide which contains an amino acid bearing a trifluoroethyl group bonded to the N-alpha position, in order to gain information about the local magnetic environment on the N-terminal amino acid. The source of this possible motivation to modify the references as suggested has not been found by the Applicants. In fact, Applicants submit that such a modification, that is, labeling the N-terminal amino acid of the peptides, as suggested in the Office Action, would be not only counter-productive to the teachings of the references, but would render the prior art unsatisfactory for its intended use. All peptides contain a terminal amino acid that includes an N-terminal nitrogen, and labeling of this nitrogen would not enable the differentiation of one peptide from another, which is the very point of the references. Absent the teachings of the present disclosure, there is no motivation found to modify the references as suggested in the Office Action. As such, Applicants respectfully submit that claim 31 patentably defines over DesMarteau in view of McDowell or Hoeltzi or Duewel.

It is believed that the present application is in complete condition for allowance, and favorable action is therefore respectfully requested. Should any issues remain after consideration of the present amendment, however, Examiner Lukton is invited and encouraged to telephone the undersigned at his convenience.

Please charge any additional fees required by this Response to Deposit Account No. 04-1403.

Respectfully submitted,

DORITY & MANNING, P.A.

Date: 11/24/03

BY: _____

Christina L. Mangelsen, Patent Agent
Registration No. 50,244
DORITY & MANNING, P.A.
P.O. Box 1449
Greenville, SC 29602-1449
(864) 271-1592